





APPROVED (1.G. F.IG.
BY CLASS SUBCLASS
ORAFISMAN

10 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Tyr Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Tyr Pro Gly Gln Gly Leu Glu Trp Met Gly Ile Ile Asn Pro Gly Gln Gly Leu Glu Trp Ile Gly Trp Ile Pro Glu Gln Gly Leu Glu Trp Ile Gly Trp Ile Asp 65 70 Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Pro Lys The Gln Gly Arg Val Thr Met Thr Arg Asp Pro Lys Phe Gln Gly Lys Ala Ser Ile Thr Ser 85 Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala 105 110

Thr Ser Ser Phe Asp Phe Trp Gly Gln Gly Thr Thr
CDR 3
Thr Ser Ser Phe Asp Phe Trp Gly Gln Gly Thr Thr
/ J>>



I G. I B PROPRO

APPROVED O.C. FIG.

BY CLASS SUBCLASS
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15 20 Lys Pro Gly Ala Ser Val Lys Val Human HV3 VH Lys Pro Gly Ala Ser Val Lys Val "CDR Grafted" VH Arg Pro Gly Ala Leu Val Lys Leu Murine 1308F VH 40 35 Tyr Met His Trp Val Arg Gln Ala Tyr Ile Tyr Trp Val Arg Gln Ala Tyr Ile Tyr Trp Val Lys Gln Arg 55 60 Pro Ser Gly Gly Ser Thr Ser Tyr Pro Glu Asn Gly Asn Thr Val Phe Pro Glu Asn Gly Asn Thr Val Phe 75 80 Asp Thr Ser Thr Ser Thr Val Tyr Asp Thr Ser Thr Ser Thr Val Tyr Asp Thr Ser Ser Asn Thr Ala Tyr 100 Val Tyr Tyr Cys Ala Val Tyr Tyr Cys Ala <u>Tyr Tyr gly</u> Val Tyr Tyr Cys Ala Tyr Tyr Gly 115 Leu Thr Val Ser Ser

Leu Thr Val Ser Ser Leu Thr Val Ser Ser



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FIG. 2 A

0.G. FIG.	CLASS SUBCLASS	
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Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Arg Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Arg Tyr 45 50 Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Gly Lys Ala Pro Lys Leu Leu Ile Tyr Arg Ala Asn Gly Lys Ser Pro Lys Thr Leu Ile His Arg Ala Asn Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Arg PHE Ser Gly Ser Gly Ser Gly Gln Glu Tyr Ser 85 90 Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Asp Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Phe His Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Phe His

Gly Thr Lys Leu Glu Ile Lys Gly Thr Lys Leu Glu Ile Lys

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FIG. 2B

APPROVED O.G. FIG.

BY CLASS SUBCLASS
MAFTSHAM

20 Ala Ser Val GLY Asp Arg Val Thr - Human K102 VL Ala Ser Val Gly Asp Arg Val Thr - "CDR Grafted" VL Val Ser Leu Gly Glu Arg Val Thr-Murine 1308F VL 35 Leu Ala Trp Tyr Gln Gln Lys Pro Leu Asn Trp Tyr Gln Gln Lys Pro Leu Asn Trp Phe Gln Gln Lys Pro 55 60 Ser Leu Glu Ser Gly Val Pro Ser Arg Leu Val Asp Gly Val Pro Ser CDR 2 Arg Leu Val Asp Gly Val Pro Ser 75 Leu Thr Ile Ser Ser Leu Gln Pro Leu Thr Ile Ser Ser Leu Gln Pro Leu Thr Ile Ser Ser Leu Glu Phe 95 100 Ser Tyr Ser Glu Phe Pro Tyr Thr Phe Gly Gly CDR 3 Glu Phe Pro Tyr Thr Phe Gly Gly

<<V / J>>



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CLASS SUBCLASS

BY DRAFTSMAN

APPROVED | C.C. FIG.

FIG. 34

MetAspTrpThrTrpArgValPheCysLeuLeuAlaValAlaProGlyAlaHisSerGln CCATGGACTGGACCTGGAGGGTCTTCTGCTTGCTGGCTGTAGCACCAGGTGCCCACTGCCAG gcgaattccatggactggacctggagggtc 3' 5

GTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGCCTGGAGCCTCAGTGAAGGTTTCC TACCTGACCTGGACCTCCCAGAAGACGACGACCGACATCGTGGTCCACGGGTGAGGGTC ValGlnLeuValGlnSerGlvAlaGluValLysLysProGlyAlaSerValLysValSer

<u>۔</u> س CACGTCGACCACGTCAGACCTCGACTCCACTTCTTCGGACCTCGGAGTCACTTCCAAAGG

CysLysAlaSerGlyPheAsnIleLysAspTyrTyrIleTyrTrpValArgGlnAlaPro TGCAAGGCATCTGGATTCAACATTAAGGACTACTACATTTACTGGGTGCGACAGGCTCCT

ACGTTCCGTAGACCTAAGTTGTAATTCCTGATGATGTAAATGACCCACGCTGTCCGAGGA

 ${\tt GlvGlnGlyLeuGluTrpNetGlyTrpIleAspProGluAsnGlyAsnThrValPheAsp}$ GGACAAGGGCTCGAGTGGATGGGTTGGATTGACCCTGAGAATGGTAATACTGTGTTTGAC

CCTGTTCCCGAGCTCACCTACCCAACCTAGGGACTCTTACCATTATGACAAACTG

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-1 G 3B

ProLysPheGlnGlyArgValThrNetThrArgAspThrSerThrSerThrValTyrMet CCGAAGTTCCAGGGCAGAGTCACCATGACCAGGGACACGTCCACGAGCACAGTCTACATG GGCTTCAAGGTCCCGTCTCAGTGGTACTGGTCCCTGTGCAGGTGCTCGTGTCAGATGTAC

GAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGTACTACGGTACA CTCGACTCGTCGGACTCTAGACTCCTGTGCCGGCACATAATGACACGCATGATGCCATGT ${\tt GluLeuSerSerLeuArgSerGluAspThrAlaValTyrTyrCysAlaTyrTyrGlyThr}$

AGCTCCTTTGACTTCTGGGGCCAAGGCACCACTCTCACAGTGAGCTCA SerSerPheAspPheTrpGlyGlnGlyThrThrLeuThrValSerSer

5 ggtgagagtgtcactcgagtattcctagggc TCGAGGAAACTGAAGACCCCGGTTCCGTGGTGAGAGTGTCACTCGAGTALtcctagg

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DRAFTSHAN

APPROVED O.G. FIG.

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F1 G. 4A

GTCACCATCACTGGCAAGGCGAGTCAGGACATTAATAGGTAGTTAAACTGGTACCAGCAG CAGTGGTAGTGAACGTTCCGCTCAGTCCTGTAATTATCCATAAATTTGACCATGGTCGTC ${\tt ValYhrIleThrCysLysAlaSerGlnAspIleAsnArgTyrLeuAsnTrpTyrGlnGln}$ ${\tt LysProGlyLysAlaProLysLeuLeuIleTyrArgAlaAsnArgLeuValAspGlyVal}$ AAACCCGGGAAAGCCCCTAAGCTCCTGATCTATCGTGCAAACAGATTGGTAGATGGGGTC TACCTGTACTCCCAGGGGGGAGTCGAGGACCCCGAGGACGACGAGACCGAGGGTCCACGG TTTACACTATAGGTCTACTGGGTCAGAGGAGGTGGGACAGACGTAGACATCCTCTGTCT COATGGACATGAGGGTCCCCGCTCAGCTCCTGGGGCTCCTGCTCTGGCTCCCAGGTGCC LysCysAspIleGlnMetThrGlnSerProSerThrLeuSerAlaSerValGlyAspArg **AAATGTGATATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGA** MetAspMepArgValProAlaGlnLeuLeuGlyLeuLeuLeuLeuTrpLeuProGlyAla cgcggatccatggacatgagggtcccc 181 61 121

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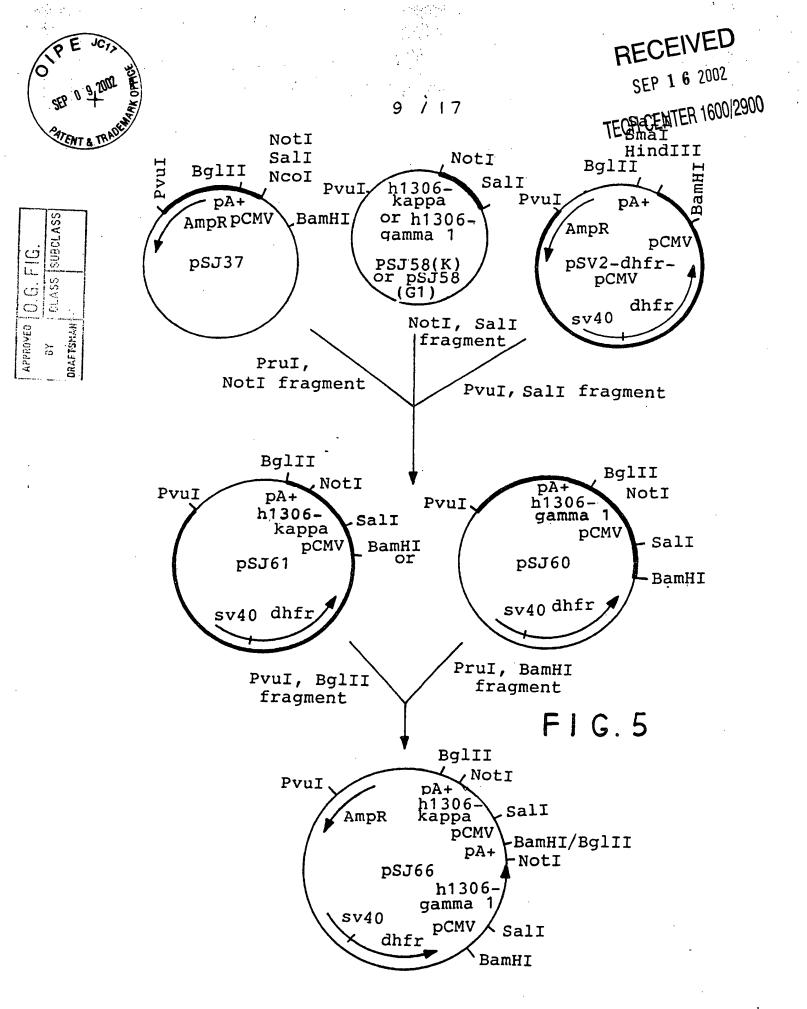


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FIG.	SUBCLASS		
- F-0	CLASS		
APPROVED	>- 30	DRAFTSMAN	

F-G. 4B

241	ProSerArgPheSerGlySerGlySerGlyThrGluPheThrLeuThrIleSerSerLeu CCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAATTCACTCTCACCATCAGCAGCCTG
301	GlnProAspAspPheAlaThrTyrTyrCysLeuGlnPheHisGluPheProTyrThrPhe CAGCCTGATGATTTTGCAACTTATTACTGCCTACAGTTTCATGAGTTTCCGTACACGTTC++++
361	GlyGlyGlyThrLysLeuGluIleLys GGAGGGGGACCAAGCTTGAAATAAAA 3'++++

cctccccctggttcgaaccc





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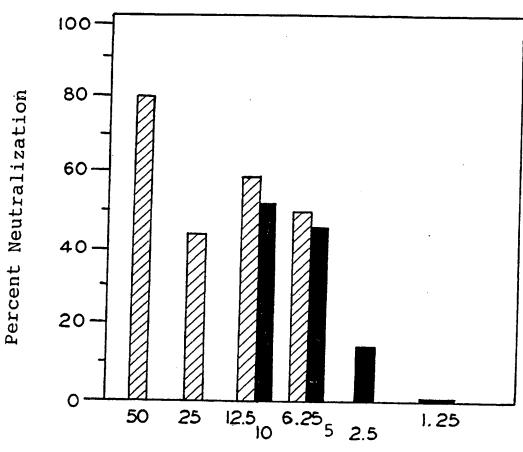
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F1G.6

■ Neut with Cos Hu

☑ Neut with 1308F Mu



Ng Mab per Reaction

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SUBCLASS

CLASS

7.9

DRAFTSMAH

APPROVED O.G. FIG.

FIG. 7A

HΛ Ser Murine 1129 VH Human VH (Cor) Leu Val Lys Pro Thr "Humanized" * * * Gin Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Leu Gln Pro Ile Gly Pro Ala Gly Pro Gly Glu Ser Glu Ser Arg Gln Leu Glu Leu ThrVal Val Gln Gln

Ser Ser Leu Gly Phe Gln Yhr Leu Thr Leu Thr Cys Thr Phe Ser 16

Ser Leu Leu Ser Ser Phe Phe $_{
m G1y}$ G1ySer Ser Phe Phe Thr Ser Cys Cys Thr Leu Thr Leu Thr Ser ren Leu Thr Thr Gln Gln

Gly Met Cys Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Gln Pro Pro Gly Lys G1ySer Gln Pro Arg Ile Arg Ile Trp Trp G1yGly Met Ser Val Gly Val Ser Met G1ySer Ser Ser Thr Thr 31

Asp Trp Leu Ala Asp Ile Glu Trp Asp Asp Lys Trp Trp Asp Asp Lys Asp Ile Trp Leu Ala Glu Glu Len Ala Leu Ala * 46

Trp Trp Asp Asp Lys Lys Asp Glu Trp Leu Ala Asp Ile Leu Gly

Gly



Ser

Ser

Thr Val

Thr Val

Gly Thr

Trp Gly Ala

Tyr Phe Asp Val

SUBCLASS 0.G. FIG. CLASS ORAF15MAH APPROVED |

F1G. 7B

Thr Thr Thr Asp Ile Ser Lys Asp Asp Lys Lys Ser Ser $_{\rm Ile}$ Ile Thr Thr Ser Leu Asp Thr Arg Leu Thr Len Len Arg Arg Ser Ser LysLeu Lys Leu Ser Ser Pro Pro Tyr Asn Thr Asn Asn $\mathbf{T}\mathbf{y}\mathbf{r}$ Tyr 61

Ala Ala Ala Thr Asn Met Asp Pro Pro Thr Asp Asp Met Val Asn Gly \mathtt{Thr} Thr Ile Val Asn Gln Val Val Leu Thr Val LysVal Leu Lys Leu Phe Asn Gln Val Gln Val Asn Lys Lys Ser Ser Ser 9/

Pro Ala Ile Pro Ala Trp TrpAsn Asn Thr Thr Ile Ile Val Yhr Met Met IleSer Ser Arg Arg Arg Ala Cys Ala Cys Ala Cys TyrTyrTyrTyrTyr Tyr Thr \mathtt{Thr} Thr Ala Ala Ala Thr Thr \mathtt{Thr} Asp Asp 91

Asb

Ser Ser Ser Ser Val Pro Val Thr Val \mathtt{Thr} Thr Val Thr Ala Gly Thr Gly Arg $_{
m G1y}$ Trp Gly Trp Asp Val Asp Val Phe Met Tyr Tyr 106



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APPROVED O.G. FIG.

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·	- Human K102 VL	- "CDR Grafted" (SEC ID 35)	- Murine 1129 VL	(SEQ ID 35)						
7.	Val	Val *	Pro	30	Ser	*	Gly	G1y	45 Lys	Lys
	Ser	Ser	Ser		Ile	×	Val	Val	Pro	Pro
4	Ala	Ala	Ala		Ser		Ser	CDR 1 Ser Val	Ala	Ala
FIG.8A	Leu Ser Ala Ser	Gln Ser Pro Ser Thr Leu Ser Ala Ser Val	Met Ser Ala Ser		Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser	×	Ile Thr Cys Lys Cys Gln Leu Ser Val Gly	<pre>x x x x CDR 1 Ser Ala Ser Ser Ser Val Gly</pre>	45 Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys	Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
<u>C</u>	Leu	Leu *	Met		Ser	×	Gln	Ser	$_{ m G1y}$	Gly
щS	Thr	$_{\star}^{\mathrm{Thr}}$	Ile	25	Ala	×	Cys	Ala	40 Pro	Pro
		Ser	Ala		Arg	ĸ	Lys	Ser	Lys	Lys
	Pro	Pro	Pro		Cys		Cys	Cys	Gln	Gln
	Gln Ser Pro Ser	Ser	Gln Ser Pro Ala		\mathtt{Thr}		Thr	Met Thr Cys	Gln	Gln
	Gln		Gln		Ile		Ile	Met	Tyr	Tyr
Ŋ	Thr	Thr	Thr	20	\mathtt{Thr}		Thr	Thr	35 Trp	Trp
	Met	Met *	Leu		Val		Val	Val	Ala	
	Gln	Gln	Gln		Arg		Arg	Lys	Leu *	His
	Asp Ile Gln Met Thr	Asp Ile	Asp Ile		Gly Asp Arg Val Thr		Gly Asp Arg	Glu	Ser Trp Leu Ala * * *	Met
	Asp	Asp	Asp		G1y		$_{ m G1y}$	Gly Glu	ser *	Tyr

Leu Trp

50 55 Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser * * *

Ser Thr Ser Pro Lys

Trp Tyr Gln Gln Lys Ser

Tyr Met His



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F1 G. 8B

APPROVED O.G. FIG.

							Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	Phe Gly Gly Thr Lys Leu Glu Ile Lys
75 Ile	Ile	Ile	90 Gln	Gln	Gln	105	Glu 1	Glu 1
	Thr	\mathtt{Thr}	Gln	Phe	Phe		Leu	ren
Thr Leu Thr	ren	Leu	90 Tyr Cys Gln Gln	Cys	Thr Tyr Tyr Cys Phe Gln		Lys	Lys
Thr	$\operatorname{Thr}_{ au}$	Ser	Tyr	Tyr	Tyr		Thr	Thr
Phe	Phe	Tyr	Tyr	Thr Tyr	Tyr		G1y	G1y
70 Glu	Gly Thr Glu	Ser	85 Thr	Thr	Thr	100	Gly	$_{ m G1y}$
Thr	$\operatorname{Thr}_{\star}$	Asn	Ala	Ala	Ala		G1y	G1y
65. er Gly Ser Gly Thr	Gly	er Gly Ser Gly Asn	Asp Asp Phe Ala	Phe *	Val		Phe	Phe
Ser	Ser	Ser	Asp	Asp	Asp		Thr	Thr
$_{ m G1y}$	er Gly Ser	G1y	Asp	Asp *	Glu		Phe	Phe
65 Ser	Ser	Ser	80 Leu Gln Pro	Leu Gln Pro Asp Asp Phe Ala	Ile Gln Ala Glu Asp Val Ala	95 Ser *	Pro	Gly Ser Gly Tyr Pro Phe Thr
Ser Gly Se	Arg Phe Ser Gly So	Gly Se	Gln	Gln	Gln	Tyr Asn Ser Tyr Ser	Tyr	Tyr
Ser	Ser	Ser	Leu	Leu *	Ile	Ser *	Gly Ty	G1y
Arg Phe	Phe	Phe	Ser	Ser	Ser	Asn *	Ser	Ser
Arg	Arg	Arg	Ser	Ser	Ser	Tyr *	<u>G1y</u>	Gly

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E X

DRAFTSMAN

APPROVED O.G. FIG.

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- GATA

CCCCCAGGGAAGGCCCTGCACTCGCTTGCAGACATTTGGTGGGGATGACAAAAAGGACTAT

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3'-GGAGTGTGACTGG

9

SJ150 5'-CCAG

ATGGACTGGACCTGGAGGGTCTTCTGCTTGCTGGCTGTAGCACCAGGTGCCCACTCCC-3"

5'-GGCGTCGACTCACC-

SJ153

F1G.9A

GTCACCTTAAGGGAGTCTGGTCCTGCTGGTGAAACCCACACAGACCCTCACACTGACC

61

 ${\tt ValThrLeuArgGluSerGlyProAlaLeuValLysProThrGlnThrLeuThrLeuThr}$

TGCACC-3

121

ACGTGGAAGAGCCCAAAAGTGACTCGTGAAGACCATACTCACATCCGACCTAAGCAGTC

 ${\tt CysThrPheSerGlyPheSerLeuSerThrSerGlyMetSerValGlyTrpIleArgGln}$

MetAspTrpThrTrpArgValPheCysLeuLeuAlaValAlaProGlyAlaHisSerGln

17

180

5'- CAG

SJ151

ProProGlyLysAlaLeuGluTrpLeuAlaAspIleTrpTrpAspAspLysLysAspTyr

GGGGGTCCCTTCCGGG-5' SJ149

181



0.00 PT SMAN

APPROVED O.G. FIG.

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F | G | 9 E

301	AATCCATCCCTGAAGTTAGGTACCGACTTCJ ASnProSerLeuLyss CTTAAAGTGACCAACPGAATTTCACTGGTTG- LeuLysValThrAsnM TAGTGCTTGACGATGA	360
	STIP STIP STIP STIP STIP STIP STIP STIP	SJ14
	${\tt IleThrAsnTrpTyrPheAspValTrpGlyAlaGlyThrThrValThrValSerSer}$	TE



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F1 G.10

- O humanized 1129
- Chimeric 1129

